PREVALENCE OF CYTOMEGALOVIRUS IN BLOOD RECIPIENT CANCER PATIENTS OF INMOL, LAHORE, PAKISTAN. (A CASE STUDY)

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ABSTRACT: *Human cytomegalovirus (HCMV) is a ubiquitously distributed pathogen that causes severe disease in immunosuppressed patients and infected newborns. The present study was carried out to determine the prevalence of CMV IgM in blood recipient cancer patients. For this purpose, thirty-four serum samples were collected from the blood recipient cancer patients at the Institute of Nuclear Medicine and Oncology Lahore (INMOL) Pakistan. All blood samples were tested by Enzyme-Linked Immunosorbent Assay (ELISA). This study showed that 26.4% of patients were positive for CMV IgM antibody. We suggest screening of blood donor samples for CMV IgM antibody before transfusion and use of other strategies like leucoreduction, filtration, saline-washed RBCs, frozen deglycerolized RBCs could be more appropriate to minimize the risk of transmission of CMV IgM antibody through infected blood to immunosuppressed recipient patients.*

Key Words: Cytomegalovirus, ELISA, Blood recipients**.**

INTRODUCTION

Infection by cytomegalovirus (CMV) is a major cause of morbidity among immunosuppressed patients, especially after solid organ transplantation. The risk of CMV after organ transplantation is strongly related to the serology of the donor and the recipient [1]. CMV infection can also be transmitted sexually via semen, cervical and vaginal secretions and through blood products [2].

Cytomegalovirus-specific immunoglobulin M is a sensitive indicator of a recent CMV infection [3]. CMV IgM in serum can be detected by different techniques but most commonly used is enzyme-linked immunosorbent assay abbreviated as ELISA [4].

HCMV genes and proteins have been found in different types of human cancers [5], including breast cancer [6], prostate cancer [7], mucoepidermoid carcinoma of salivary gland [8], glioblastoma [9] and medulloblastomas [10]. Secretion of cytokines and growth factors caused by HCMV infection promote carcinogenesis [5].

The Society of Obstetricians and Gynaecologists of Canada published an article which showed that there was only 30 – 40 % probability of intrauterine transmission, only 1% after secondary infection [11]. A case study from North India among multitransfused recipients revealed the seropositivity for IgM antibodies. Out of 200 patients seroprevalence for anti-CMV IgG antibodies was in 100% patients and only one was positive for anti-CMV IgM antibody [12]. A study in Sudan on 98 kidney transplant patients demonstrated that HCMV IgM antibodies were found in 6.1 % of patients [13]. Study of acute CMV infection in liver transplant recipients concluded that CMV IgM seropositivity was independently associated with increased short term risk of venous thromboembolism (VTE), following for other confounding factors and age [14].

In Pakistan, the seroprevalence of CMV in blood recipient patients has not yet been documented. The blood recipient patients are at high risk for CMV infection. Therefore, our basic aim is to determine the prevalence of CMV in blood recipient patients by detecting CMV IgM antibodies. This study will help in developing proper strategies for reducing CMV infection through blood transfusion, especially in immunocompromised patients.

MATERIALS AND METHODS

The present study is based on 34 blood recipient cancer patients admitted over a three month period from December to February at the Institute of Nuclear Medicine and Oncology Lahore (INMOL), Pakistan. Blood samples of all 34 blood recipient cancer patients were collected and sera were separated and stored at -40 ºC. CMV specific IgM was detected by using Enzyme Immunoassay (ELISA) for the Detection of IgM Antibodies. For this purpose, commercially available CMV Ig M kit, Biocheck Inc., USA (Cat log No. BC-1091) was used. Purified CMV antigen was coated on the surface of microwells and diluted serum was added to them. If CMV IgM specific antibody was present, it would bind to the antigen and all unbound materials was washed away with wash buffer. Later on, HPR-conjugate was added, which binds to antigen-antibody complex whereas excess HPR-conjugate was washed off and later a solution of TMB reagent was added. The enzyme conjugate catalytic reaction was stopped at a specific time. The intensity of the color generated is proportional to the amount of IgM specific antibody in the sample. The tests were performed and results were read by microwells reader. The CMV IgM index of blood recipient cancer patient samples were used to interpret the results. The patient samples have IgM index 1.0 or greater were positive for IgM antibody to CMV, while patient samples have CMV IgM index less than 0.90 were negative. The patient samples of CMV IgM index between 0.91-0.99 were equivocal [15,16,17].

RESULTS

A total of 34 blood recipient cancer patients were screened for CMV IgM. All subjects were male and female blood recipient cancer patients. CMV IgM was positive in 9 blood recipient cancer patient samples while 25 samples were negative for CMV-specific IgM antibodies (Table 1). The mean age of the recipient was 40.26 ±1.53 years. Out of a total of 34 samples, 14 (41.17%) were males and 20 (58.82%) were females. Out of 9 positive samples, 5 were females (55.5%) and 4 were males (44.4%). During our study, we found that all recipient patients were suffering from various kinds of cancers. Among these patients 5 were

suffering from lymphoma (14.7%), 5 from sarcoma (14.7%), 6 from leukemia (17.6%) and 17 were suffering from other types of cancer including breast, colon, liver, lung, cervix and ovarian cancer (50%). Hence, the prevalence of CMV IgM among blood recipient cancer patients was 26.4% (Table 1).

Table 1: Seroprevalence of CMV-specific IgM antibodies among blood recipient cancer patients.

Status	Anti CMV- IgM screened	%age
Positive	9	26.4%
Negative	25	73.5%
Total	34	100%

DISCUSSION

In our study on the prevalence of cytomegalovirus IgM antibody, all subjects were male and female blood recipient cancer patients. A total of 34 blood recipient cancer patients were screened for CMV IgM with the help of Enzyme-Linked Immunosorbent Assay (ELISA). CMV IgM was positive in 9 blood recipient cancer patients while 25 samples were negative for CMV IgM among blood recipient cancer patients. Hence the seroprevalence of CMV IgM among blood recipient cancer patients was 26.4%.

The results of the present study are comparable with some previous studies. Prevalence of anti-CMV IgM was 24% in multiple transfused group in Bangladesh which is significantly higher [18]. A study in Germany revealed that transfusion-transmitted CMV (TT-CMV) possibly dangerous complication of transfusion therapy in immunodeficient patients, the CMV IgM prevalence rate was 17.0% observed in patients undergoing hemodialysis [19]. A study carried out in Delhi, India seroprevalence of CMV IgM rate among multitransfused children was 3.1% before the post-implementation period and 15.6% during the pre-implementation period [20].

In the present study, the prevalence of CMV is 26.4% in blood recipient cancer patients which is higher than 8.57% estimated in blood donors [21]. This high prevalence of CMV in blood recipient compared with blood donors might be due to transfusion of CMV seropositive blood in these patients. Some studies suggest there is a relationship between transfusion and CMV antibody seropositivity [22]. One such report demonstrated that CMV can be transmitted through transfusion with a frequency of about 0.14% to 10% per unit of blood [23]. Studies from India also reported CMV infection in neonates after exchanging transfusion [24]. It has been reported that recipient factors such as CMV virus, the degree of immunosuppression, increase cytokines production are associated with TT-CMV [25]. Furthermore, it has been documented that blood transfusion itself leads to immunomodulation with a profound negative effect on the immune system which persists for many months [26]. All these indicate high risk and need for strategies in the prevention of TT-CMV.

Traditionally, preventive strategies of TT-CMV in high-risk transfusion recipients are a transfusion of CMV free or CMV "safe" prestorageleucodepleted blood components [27]. Leucodepleted blood product reduces the risk of CMV by reducing the number of the latently infected cell of blood components, in addition, it reduces the possibility of CMV reactivation in recipients by reducing cytokines release and another immunological trigger from donor leucocytes [28]. The American Association of Blood Banks has recommended transfusion from donors who are seronegative for CMV or the use of deglycerolized frozen RBCs whenever transfusion contemplated in a seronegative preterm child born to a mother with negative or unknown immune status with regard to CMV infection [29]. These guidelines have helped in eliminating transfusion-induced CMV infection syndrome in preterm infants in the West.

Other preventive strategies, such as leukoreduction, filtration, saline-washed RBCs, frozen deglycerolized RBCs etc are being increasingly recommended to minimize the transmission of CMV through transfusion [30].

The limitations of this study are small sample size (due to the financial problem in purchasing enough test kits). Despite this limitation; the present study shows the seroprevalence of anti-CMV IgM among blood recipient patients.

Therefore, we suggest screening of blood of donors for CMV positivity before transfusion and identify the seronegative blood donors in the population and keep a record of them so that they can be called upon when needed for blood transfusion in patients. It is also suggested that if seronegative blood is not available then any of the above-mentioned methods should be adopted to make the blood free from CMV before transfusion to a recipient patient to prevent the risk of transfer of CMV from a blood donor to recipient patients.

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